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ASIA BRACES FOR EBOLA

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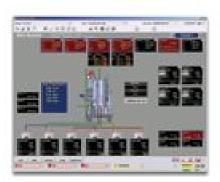
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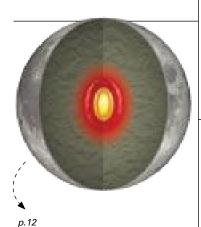
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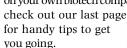
EDITOR'S NOTE

The January 2015 issue of Asian Scientist Magazine is dedicated to all things biotechnology. We look at all stages of the pipeline, from emerging problems that demand a robust technological solution (Ebola), to exciting new technologies that look set to revolutionize the field (optogenetics); products that are close to commercialization and even those that are market ready (Asian biotech innovations).

While technology has the clear potential to impact lives, our articles highlight that technology alone is insufficient. Political will, affordability and even a supportive intellectual property infrastructure all interact to determine whether a given biotechnology fails or succeeds.

At the personal level, we hear from Dr. Kiran Mazumdar-Shaw, founder of Biocon, on her own journey in building what is now India's largest biotechnology firm. Mr. Goh Khoon Seng from Edwards Lifesciences also shares with us what it takes to be a great medical device company.

We hope that you'll find this issue as fascinating and insightful as it has been for us putting it together. If you've been inspired to get started on your own biotech company,



Cheers!

Rebecca Tan | Managing Editor



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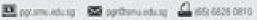
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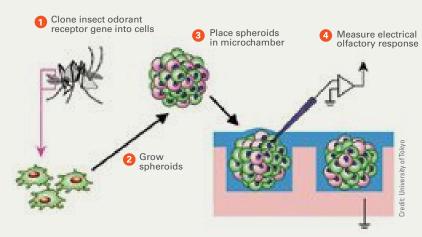












HOW TO BUILD AN ARTIFICIAL 'NOSE'

Scientists have developed the

first artificial 'nose' that can sense chemical vapors. Their results have been published in Angewandte Chemie International Edition.

Recreating odorant receptor (OR) sensing is complicated as it requires researchers not only to introduce the OR itself, but also all downstream signalling proteins. The key to their success was the use of insect OR, which are ligand gated ion channels that directly cause cell depolarization upon activation.

"This molecular characteristic meant that insect OR could be studied without the need to reconstitute G-protein subunits, effectors and downstream ion channels, making them particularly suitable for the development of protein-based olfactory sensors," lead author Dr. Koji Sato told Asian Scientist Magazine.

Using insect OR expressed on a tiny ball of cells, Sato and his team at the University of Tokyo were able to show differences between responses to smells in vivo and in vitro, suggesting that compounds in the mucus affect the mechanism of odor recognition.

GENE EDITING DOES NOT INTRODUCE NEW MUTATIONS

New gene editing technologies are creating a stir in the biological sciences. But are they safe enough to be used in humans?

"As cells are being reprogrammed into stem cells, they tend to accumulate many mutations," said Dr. Li Mo from the Salk Institute, co-first author of the study published in Cell Stem Cell. "So people naturally worry that any process you perform with these cells in vitro-including gene editing-might generate even more mutations."

Using an existing gene editing technology called helper-dependent adenoviral vectors in combination with the newer TALEN technology. a team including researchers from BGI and the Chinese Academy of Sciences edited out the mutated gene that causes sickle cell disease from a human cell line. Genome sequencing showed that cells that had undergone gene editing had no more mutations than the cells kept in culture.

"We found less than a hundred single nucleotide variants in all cases." said co-first author of the study. Dr. Keiichiro Suzuki, also from Salk.

DEEP DOWN, THE MOON IS STILL WARM

Contrary to expectations, research published in Nature Geoscience suggests that the moon has a warm inner core.

But how do scientists know the internal structure of a celestial body far away from us? One way is to study the shape—or tide—of the celestial body as it changes in response to gravitational forces exerted by other nearby bodies.

A research team led by Dr. Yuji Harada from the China University of Geosciences performed theoretical calculations and found that the observed tidal deformation of the moon can be well explained if it is assumed that there is an extremely soft layer in the deepest part of the lunar mantle.

Furthermore, they also showed

that tides generated in this soft layer efficiently generate heat. This finding implies that that the soft layer acts as a thermal blanket, wrapping around the core of the moon and keeping it warm.

BLUE IS THE WARMER COLOR

A study published in *Scientific Reports* shows that blue objects are more likely than red objects to be judged as warm, defying intuitive expectations.

Dr. Ho Hsin-Ni from NTT Communication Science Laboratories, together with colleagues from Osaka University, found that blue objects were perceived to be an average of 0.5°C warmer than red objects.

"When we look at a blue object, we expect it to be cold, because blue signifies cold," explained Ho. "Since our brains anticipate a cold blue object, the actual temperature perception

would be higher than the expectation and this contrast would make a blue object feels warmer than it actually is. Similarly, when we look at a red object, we anticipate a warm red object. Since the actual temperature perception would be lower than expectation, a red object would feel not as warm."

These findings suggest that when confronted with differences between expectation and reality, the brain contrasts rather than averages the differences. The group are studying how other visual cues besides color influence tactile perception of temperature and surface roughness.

MATERIALS SCIENCE

STRONGER MATERIALS BASED ON SQUID SUCKERS



Unlike hard tissue such as bone, squid sucker ring teeth (SRT) are made entirely of proteins and do not contain any additional minerals for strength. Known as suckerins, these proteins form the razor-sharp teeth of cephalopods and could be used to design strong and malleable biomaterials.

A research team led by Assistant Professor Ali Miserez from Nanyang Technological University has now identified 37 additional SRT proteins from two squid species and a cuttlefish. In a paper published in the journal ACS Nano, they describe the architecture of the SRT proteins, including how their components form what is known as \(\mathbb{B} - \mathsec{sheets}, a \) structure which gives spider silk its unusual strength.

"We envision SRT-based materials as artificial ligaments, scaffolds to grow bone and as sustainable materials for packaging, substituting for today's products made with fossil fuels," said Miserez.

IMMUNOLOGY

DECODING DENGUE'S COUNTER ATTACK

Researchers from Duke-NUS Graduate Medical School have discovered a new mechanism used by dengue virus-2 (DENV-2) to suppress the body's immune response.

The team first identified three host RNA binding proteins—G3BP1, G3BP2 and CAPRIN—that provide a powerful antiviral response to infections. They then went on to show that DENV-2 produces large quantities of a non-coding, highly-structured viral RNA termed subgenomic flaviviral RNA.

The viral RNA acts as a sponge by soaking up host RNA binding proteins, in the process disabling host immunity.

"We not only found a new way in which the pathogen (dengue virus) interferes with the host response (human immune system), we also uncovered the first mechanistic insight into how this non-coding RNA works. This discovery opens the door to explore therapeutics through this channel," said Prof. Mariano Garcia-Blanco, senior author of the study.



THE LINK BETWEEN CARDIOVASCULAR DISEASE AND



Incense Use

Daily incense use is associated with a higher mortality rate due to cardiovascular disease, according to a study of over 63,000 Singaporean Chinese published in Environmental Health Perspectives.

By tracking the number of cardiovascular deaths through the national death registry, a team of researchers led by Associate Professor Koh Woon-Puay from Duke-NUS Graduate Medical School predicted that chronic exposure to incense smoke may account for eight percent of the deaths due to coronary heart disease and 12 percent of the deaths due to stroke.

Incense burning releases volatile organic compounds and particulate matter that could be harmful to health. Although their intention is not to discourage the burning of incense for religious reasons, the authors hope to educate users about the possible effects of incense use on their health and encourage behaviors that reduce exposure to incense smoke.

Asian Ancestry

Asians suffer from heart failure at least ten years earlier than their Western counterparts, according to a study of heart failure patients in 11 Asian countries. These findings were presented by National University of Singapore Associate Professor Carolyn Lam at the European Society of Cardiology Heart Failure Congress in Athens, Greece.

According to Lam: "The frightening finding is that heart failure affects Asian patients at a much younger age than in Western countries, and within Asia itself there is tremendous diversity in disease characteristics."

Lam pointed out that the average ages of patients from China, India and Malaysia are even younger than 60 vears and the rates of diabetes are strikingly high among patients from Singapore and Malaysia. The disease affects almost 60 percent of patients in Singapore and almost 50 percent of those from Malaysia, compared to only 33 percent of patients in Europe.

"These findings have important implications for risk factor control and treatment for the prevention of heart failure," she explained.

Instant Noodles

A study of over 10,000 South Koreans has shown that a diet high in convenience food-including instant noodles-may increase the risk of cardiometabolic syndrome in women. This research has been published in the Journal of Nutrition.

"While instant noodle intake is greater in Asian communities, the association between instant noodle consumption and metabolic syndrome has not been widely studied," said lead author Dr. Shin Hyun Joon. a doctoral student at the Harvard School of Public Health.

Shin found that eating instant noodles two or more times a week was associated with cardiometabolic syndrome, but this was only true for women and not men. He said that this result could be attributed to biological differences such as sex hormones and metabolism.

Another potential factor in the gender difference is a chemical called bisphenol A (BPA), which is used for packaging the noodles in styrofoam containers. BPA is thought to interfere with the way hormones send messages through the body.





HOW YOU **MEDITATE MATTERS**

Not all meditation techniques produce similar effects on the body and mind, a study has found.

The research team of Associate Professor Maria Kozhevnikov and Dr. Ido Amihai from the National University of Singapore collected electrocardiographic (ECG) and electroencephalographic (EEG) responses and also measured behavioral performance on cognitive tasks by experienced Theravada and Vajravana meditation practitioners.

They found that Theravada meditation produced enhanced parasympathetic activation (relaxation), making it a useful way to decrease stress and release tension.

In contrast, Vairavana meditation did not show any evidence of parasympathetic activity but showed an activation of the sympathetic system (arousal). Furthermore, Vajrayana meditation led to a dramatic enhancement in cognitive performance, suggesting that it could be especially useful in situations where it is important to perform at one's best, such as during a competition or states of urgency.

DETOX WITH BROCCOLI SPROUT JUICE

A team of scientists from China and the US has shown that drinking half a cup of broccoli sprout beverage every day results in rapid, significant and sustained levels of air pollutant excretion from the human body.

Broccoli sprouts are known to contain high levels of glucoraphanin, which, in conjunction with the enzyme myrosinase, produces sulforaphane that helps remove air pollutants from the body.

To investigate whether broccoli sprouts could improve the health of people living in polluted environments, the team conducted a clinical trial involving 300 Chinese participants residing in Qidong city, along the Yangtze River delta region of China.

The study, which was published in Cancer Prevention Research, found that participants who took the broccoli sprout beverage passed out 61 percent more metabolized benzene in their urine. The participants also excreted detoxified acrolein, a lung irritant, at a rapidly increasing rate within the 12-week study.

SHORTER SLEEP, **FASTER AGING**



Researchers at Duke-NUS Graduate Medical School have found evidence that the less older adults sleep, the faster their brains age. These findings, published in the journal SLEEP, pave the way for future work on sleep loss and its contribution to cognitive decline, including dementia.

The study examined the data of 66 older Chinese adults from the Singapore-Longitudinal Aging Brain Study. Participants underwent structural MRI brain scans measuring brain volume and neuropsychological assessments testing cognitive function every two years. Additionally, their sleep duration was recorded through a questionnaire. Those who slept fewer hours showed evidence of faster ventricle enlargement and decline in cognitive performance.

"Our findings relate short sleep to a marker of brain aging," said Dr. June Lo, lead author of the study and a Duke-NUS research fellow.





BIRDS SHOW INNATE FRUIT COLOR PREFERENCE

Tropical Asian birds

seem to favor red and black fruits, suggesting that fruit color evolution is partially influenced by bird preferences.

Professor Quan Rui-Chang, who works at the Xishuangbanna Tropical Garden under the Chinese Academy of Sciences, tested the behavior of four species of fruit eating birds in response to artificial and natural fruit colors. Artificial fruits were made from a mixture of fruits and corn flour, and were dyed black, red, yellow, green or blue, matching the colors of the natural ripe fruits used.

"The most interesting finding was that the preferences of hand-raised birds more accurately reflected the colors of fruit found in nature than wild-caught adults. The hand-raised birds preferred black natural fruits. which is the most common color," Ouan told *Asian Scientist Magazine*.

"It makes sense from an evolutionary perspective that young birds should innately prefer common fruit colors as this would quickly lead them to find food," he explained.

JAPANESE CATFISH USE PH TO LOCATE PREY

The Japanese sea catfish Plotosus japonicus has a neat trick for finding prey in dark murky water: it uses pH. Published in Science, this study is the first report of any fish using pH to find live prey.

Catfish respond to changes in pH caused by sea worms as they breathe and release tiny amounts of carbon dioxide and acid, the study found. Using infrared photography, the team showed that the nocturnally active fish spent significantly more time in the vicinity of the worms than in other locations in the aquarium. The fish also attacked tubes emitting seawater of a slightly lower pH even when no worms were present.

"These fish are like swimming pH meters. They are just as good as a commercial pH meter in the lab," said Professor John Caprio, who conducted the research with colleagues from Kagoshima University in Japan.

These findings imply that the food-locating abilities of Japanese sea catfish could be compromised by ocean acidification, caused in part by man-made activities.

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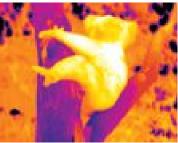
TREEHUGGING IS COOL

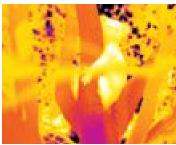
Research published in the iournal Biology Letters shows that koalas (Phascolarctos cinereus) use tree hugging to cope with extreme heat.

Researchers used thermal imaging to measure what the koalas were experiencing in the places they chose to sit compared to the places available to them. They found that the trunks of some tree species could be over 5°C cooler than the air during hot weather.

"Cool tree trunks are likely to be an important microhabitat during hot weather for other tree dwelling species including primates, leopards, birds and invertebrates. The availability of cooler trees should be considered when assessing habitat suitability under current and future climate scenarios," said Dr. Michael Kearney, co-author of the study from the University of Melbourne.







Thermal images of a koala hugging a tree trunk or lying on the lower limb of an Eucalyptus ovata tree during hot weather. (Photo Credit: Steve Griffiths)



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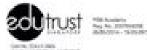
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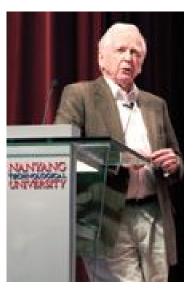
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From left to right:

1. Global Young Scientist Summit (GYSS) 2. The University of Tokyo 3. National University of Singapore



SENIOR SCIENTISTS TO ATTEND **SINGAPORE YOUTH SUMMIT**

More than 300 young scientists from all over the world will gather in Singapore to hear from and engage with world class researchers at the Global Young Scientist Summit (GYSS), held from January 18-23, 2015.

This year's star-studded line up will see new faces such as 2010 Fields Medalist Ngô Bảo Châu and 2014 Millennium Technology Prize winner Stuart Parkin.

Launched in 2013 to inspire talented graduate students and post-doctoral fellows below the age of 35 to apply themselves to the interdisciplinary challenges of tomorrow, the five day program will address key areas in science, research and technology innovation.

Ten finalists will also compete for a cash prize of US\$100,000 and the Singapore Challenge Medal with their research proposals on the topic of Aging-in-Place. They will propose solutions that help seniors stay close to their communities even as diseases and frailty set in.



JAPAN LEADS ASIA IN ASIA-PAC UNIVERSITY **RANKINGS**

The University of Tokyo and Kyoto University have retained their top positions in the 2014 Academic Ranking of World Universities (ARWU), coming in 21st and 26th respectively.

The ARWU ranks universities according to six parameters; whether the staff or alumni of the institution has won a Nobel prize or Fields medal, number of papers published in the journals Nature and Science, number of article citations, number of researchers on the Thomson Reuters highly cited list and per capita performance of the institution.

Peking University, Tsinghua University and Shanghai Jiaotong University were China's leading institutions, ranked within the top 150 in the world.

Seoul National University was the only Korean institution among the top 150; likewise, the National University of Singapore was the only Singapore institution in the top 150.



SMALL ASIAN COUNTRIES SURGE IN OS RANKINGS

Five out of the nine Asian universities on the 2014/2015 Quacquarelli Symonds (QS) World University Ranking top 50 are based in the small island economies of Singapore and Hong Kong, with the highest ranked National University of Singapore and University of Hong Kong coming in at 22nd and 28th respectively.

The other four Asian universities to make the top 50 are the University of Tokyo and Seoul National University (joint 31st); University of Kyoto (36th); and China's Tsinghua University (47th).

Unlike other rankings which are more publication focused. the QS rankings also analyze soft data such as surveys of academics and employers.



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ASIAN BIOTECH INNOVATIONS TO WATCH IN 2015₀

FROM THE LAB TO THE MARKET

From 3D printed bones to smart shoes that buzz you to your next destination, Asian biotechnology innovations are making their impact in a wide range of applications. Yamini Chinnuswamy highlights ten of the hottest products to look out for in 2015. Remember, you read it here first!



SICKLE CELL CHIP

Sickle cell disease, where abnormally shaped blood cells have a diminished ability to carry oxygen, causes over 20,000 deaths each year.

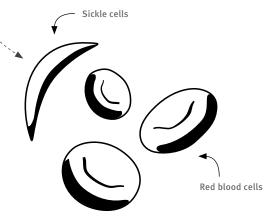
Diagnosing the disease requires expensive equipment and trained personnel, both of which are often lacking in rural areas.

Researchers from the Indian Institute of Technology, Bombay, have developed a microfluidic device to help in the diagnosis of sickle cell disease.

The microfluidic device preserves blood samples in deoxygenated conditions. If a patient has the disease, their cells will adopt the eponymous sickle shape.

Using a mobile device-based app, healthcare workers can make a quick diagnosis and send the patient for treatment.

DISEASE



30-MINUTE EBOLA TEST

In the near future, diagnosing Ebola a highly dangerous viral disease may take as little as 30 minutes and only require a small, batterypowered warmer.

Researchers from Nagasaki University in Japan are collaborating with colleagues from Eiken Chemical to develop an Ebola virus detection kit.

The kit uses short DNA sequences called primers to amplify DNA unique to Ebola. Patient samples turn cloudy if the virus is present, providing a simple visual cue for the virus.

The team is currently exploring industrial collaborations to make their technology available in Ebola-stricken countries.

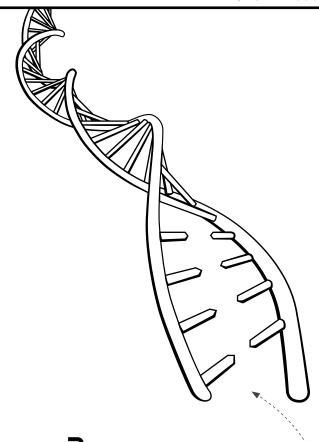


The majority of antibody drugs in clinical trials today have complex structures and high molecular weights, making them costly to manufacture.

Researchers at the Korea Advanced Institute of Science and Technology (KAIST) have made a simpler version of an antibody, called a repebody.

The artificial antibodies have a simpler structural backbone fused to a protein binding domain and can be mass produced in bacteria.

In a mouse model of non-small cell lung cancer, repebodies bound to their interleukin-6 target, leading to a reduction in tumor load.



GENE SCISSORS

Imagine being able to 'cut-and-paste' any genetic sequence at will, even in living organisms.

Thanks to a Korean company called Toolgen, we can now use genetic editing technology to 'snip' out desired stretches of DNA.

The gene editing process first introduces double-stranded breaks in diseased genes, before replacing them with good copies of DNA.

Toolgen is now working with a Korean university to increase biofuel yield from microalgae.

TOOLS ON THE GO

WEARABLE SOLAR CELLS

Chinese researchers at Fudan University have developed a new technology that can turn our clothes into walking solar batteries. The 'solar cell fabric' has already been used to power an LED light.

Thread-like solar cells that can be woven into textiles aren't a new idea. but previous versions were inflexible and costly to produce.

Instead of making wire-shaped cells, researchers decided to stack the components, layering a titanium electrode filled with light-absorbing dye over a carbon nanotube counter electrode.

The new wearable solar captures incident light at multiple angles and works well when bent, allowing them to be easily integrated into knit fabrics.

PORTABLE DNA SEQUENCER

DNA sequencing plays a major role in the diagnosis of deadly diseases, but conventional sequencers are bulky and not portable.

Researchers at New Zealand's University of Otago have now developed a handheld DNA sequencing device capable of running for up to six hours on batteries.

Freedom4 processes DNA samples in a single step and can be used to detect bacterial and viral infections within an hour.

Thanks to these advances in technology, forensics labs can finally



LIFESTYLE Enhancers

SMART SHOES

What if you could tell your phone your next destination and let your shoes lead the way?

Indian start-up Ducere Technologies has developed Bluetooth-enabled shoe technology that uses Google maps to help wearers navigate.

Called Lechal shoes, the technology was originally designed to help visually impaired individuals achieve mobility.

Developers realized, however, that the shoes—named for the Hindi phrase, "take me along"—could also be useful for tourists in a new country, or joggers along their running paths.

The World Health Organization estimates that most of the world's 280 million visually-impaired people live in developing countries such as India.

POLYMER TOOTH SPRAY

Bad breath, or halitosis, isn't just socially awkward, it is also a medical problem.

To remove the bacteria in the oral cavity, people usually resort to a combination of vigorous mouth cleaning, dietary changes or probiotic intake.

But the solution to halitosis may lie in seafood. A Taiwanese company called Toothfilm Biofilm Innovation has developed a breath freshener from chitosan, which is extracted from the exoskeleton of crustaceans.

T-Spray, as it is called, kills bacteria and removes plaque build-up. It purportedly also helps to re-mineralize tooth enamel.





Credit: Toothfilm Inc

SCIENTIFIC SOFTWARE MADE SIMPLE



In today's data-saturated world, software plays an essential role in helping scientists understand information. We catch up with **Mr. Kenneth Koh**, CEO of TechSource Systems, Southeast Asia's sole distributor of MATLAB® and Simulink®, to hear about how software has transformed the research landscape in ASEAN and beyond.

How did you get into the business of scientific software?

My interest in software began when I was a student at Singapore Polytechnic. After graduation, I joined the air force, where I was fortunate enough to be involved in software development, allowing me to practice what I learnt during my studies.

Back in 1996 when I first incorporated Tech Source, not many people appreciated the value of software, leading to rampant copyright violations. Within the realm of software itself, the database and computer aided design and manufacturing (CAD/CAM) markets were highly saturated.

Looking around for a niche, I felt that science-related software would be key to driving the future developments of the scientific world, particularly in the fields of modeling and simulation which were not very well understood at the time.

What are MATLAB and Simulink?

MATLAB and Simulink are software that are widely used by both professionals and academics to collect, analyse and visualize data. In relation to computational biology, our products provide a single, integrated environment to support pharmacokinetics, bioinformatics, systems biology, bioimage processing, biostatistics and drug discovery.



Who might use such software?

At the moment, all higher education institutions in Singapore already make use of our software and we are looking at moving down the chain from the universities to the Institutes of Technical Education.

In terms of industry, our software is widely accepted, especially in the data storage and hardware sectors. Over the recent years in ASEAN, we've also gained a foothold in the automotive industry where our software is used to design cars. Increasingly, we are seeing users working on data analytics (Big Data) problems as well.

What are some interesting applications of MATLAB and Simulink?

One area where our software is making a significant contribution is the field of product design, particularly for medical devices. For example, some have used our software to validate a medical device used in jaundice identification in newborns. Using our software can help shorten the product development cycle by as much as three times compared to the traditional design environment.

On a larger scale, I have seen users design an entire flight simulator completely within our software environment. Thanks to the in-built code generation ability, users can modify the software without relying on a programmer. Although we originally began by promoting our software to academia, the excitement has diffused to industry and we are now seeing adoption at a bigger scale.

"Software is key to driving the future developments of the scientific world."

What is your vision and strategy for your company going forward?

My vision for the future is that our software will not only be used in tertiary institutions but even be used by non-professionals.

I think this is already happening; we are seeing non-engineers such as doctors and accountants using our software to do work that may have been outsourced to programmers in the past. We have come to the point where we have tools that can be used by almost any individual, regardless of background training. Making our products easy to use helps to expand our market.

My goal is not just to concentration on professionals in engineering and mathematics, but to push to make these tools available to non-developers as well.



Authorised Distributor of



TechSource Systems

Incorporated in 1996, Tech Source Systems is committed to provide quality technology solutions that empower the engineering and R&D community, providing the ultimate computing environment for technical computation, design, simulation, visualization and implementation.

TechSource is the sole distributor in Southeast Asia for The MathWorks, Inc., developer of the MATLAB® and Simulink® family of products.

TechSource is headquartered in Singapore, with offices in Malaysia, Thailand and the Philippines.

15 A BRACES FOR **EBOLA**

Is biotech our best bet?

Juliana Chan & Yamini Chinnuswamy take a look at the options available in our medical toolbox should Ebola reach our shores.

> SIA MUST STRENGTHEN its defenses against the Ebola outbreak, urged World Health Organization (WHO) Director-General Dr. Margaret Chan. "In the simplest terms, this outbreak shows how one of the deadliest pathogens on earth can exploit any weakness in the health infrastructure," she said in a meeting with health officials.

At the time of publication, the death toll from Ebola in 2014 has passed 6.500 people across seven countries, a figure that is still rising exponentially. With the battleground seemingly spreading out of West Africa, there is no doubt that Asia cannot afford to be on anything other than the highest alert.

Deep scars from SARS

To date, Asian countries have taken a pro-active role in the fight against Ebola, sending hundreds of trained healthcare workers, millions of dollars in donations, as well as protective gear and equipment to help with the West African outbreak.

With any luck, health systems across Asia will be able to contain the outbreak, should it occur, though it would not be their first brush with imported infectious disease: in the early 2000s, the region of 1.8 billion was ground zero for severe acute respiratory syndrome, or SARS.

The SARS coronavirus spread by air-borne respiratory emissions from Hong Kong to almost 40 countries, including China, Taiwan and Singapore, within weeks of its first appearance. In the ensuing outbreak, almost 1,000 individuals died, out of over 8,000 infected people.

Can biotechnology help us?

Because of the novelty of SARS. there were no vaccines, treatments or diagnostic tests available when the outbreak hit Asia. Ebola, in contrast. has been known for decades. In the 40 years since its discovery, there have been attempts at developing a biotechnology-based solution, but a lack of market demand has confined development to a few small academic or non-profit labs, and more recently, the vagaries of investment cycles.

On September 4, 2014, the share prices of US pharma company Chimerix plunged by more than nine percent on the NASDAQ stock exchange, despite jumping almost 40 percent in the last month. News had just broken that Thomas Duncan, a Liberian man who became the first person to be diagnosed with Ebola virus disease in the US, had died. Physicians had been treating Duncan with brincidofovir, an experimental drug Chimerix had developed.

The few pharma companies already working on Ebola vaccines have also ramped up their development efforts. Some of these vaccines have entered human trials in the US, including one

by pharma giant GlaxoSmithKine. Johnson & Johnson's Crucell unit is currently working with the National Institute of Allergy and Infectious Disease (NIAID) on a modified human cold virus that carries Ebola genetic information. J&J's vaccine is expected to start human trials this year.

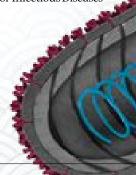
Bracing for the worst

But a vaccine developed today could end up useless, scientists say, if the Ebola virus continues evolving as quickly as it has. A Broad Institute and Harvard University study published in the journal *Science* found that the 2014 Ebola strain has accumulated far more genetic mutations than seen previously.

In addition, determining if experimental drugs work is a challenge, because the current urgency in battling Ebola has necessitated that patients receive multiple interventions at the same time. In any case, the next steps to manufacture these medicines on a large scale won't be cheap or easy.

The uncertainties of finding a drug or vaccine also highlight the importance of looking to other biomedical tools that can aid the Ebola effort. Researchers at Japan's Nagasaki University have developed a polymerase chain reaction (PCR)-based detection test that only needs 30 minutes and a battery-powered warmer. If a blood or bodily fluid sample is positive for the Ebola virus, the solution turns cloudy. providing a simple tool that could prove a boon to healthcare workers in rural field hospitals.

"Given the rapid expansion of global travel in Asia and its economic development, Asia effectively will be connected to almost every part of the world," Professor Leo Yee Sin, director of the Institute of Infectious Diseases



and Epidemiology at Singapore's Tan Tock Seng Hospital, told Asian Scientist Magazine.

"It is therefore vital for Asia to beef up its outbreak response within the region, improving outbreak research as part of its efforts. The scope of research in this area is wide. from research into the best detection methods to treatment, prevention and societal response."

Pandemic preparedness

While Asia braces itself for Ebola. it should also be remembered that the next pandemic could strike from anywhere. Thankfully, the deep scars left by SARS and the more recent H1N1 and H7N9 bird flu scares have iolted Southeast Asian countries into action. The ASEAN Working Group on

Pandemic Preparedness and Response is adapting a framework it developed from the SARS epidemic to fight the Ebola virus, should it prove necessary.

A good public preparedness framework is absolutely critical, but the right vaccine or drug could be the silver bullet that stops Ebola in its tracks. Right now, just a dozen or so biotech companies stand between us and Ebola. The failure to develop a working vaccine or treatment over the last 40 years raises the question of whether the development of much needed new therapies should be left to market incentives. Given the potential for loss of life and economic devastation. this is a question that Asia cannot afford to ignore.

Just a dozen or so biotech companies stand between us and Ebola.

What you need to know about Ebola

Ebola virus disease

Ebola virus disease (EVD), formerly known as Ebola hemorrhagic fever, is a severe, often fatal illness in humans.

How it spreads

The virus spreads from direct contact with blood and body fluids, or contaminated objects (like needles). Ebola is not spread through the air or by water.

How it kills

Ebola disarms cells of the immune system. The host launches a disorganized defense, leading to organ failure and excessive bleeding. Symptoms include fever, vomiting, diarrhea, low blood pressure and hypotensive shock.

50%

The average EVD case fatality rate is around 50%.

2 to 21 days

The incubation period from time of infection to symptoms is 2 to 21 days.

Vaccines

There are currently no licensed Ebola vaccines but two potential candidates are undergoing evaluation.

6.500

The current death toll from Ebola virus disease is 6.500.

Source: World Health Organization

THE OPTOGENETICS REVOLUTION

Illuminating the mysteries of the brain

Optogenetics promises to give neuroscience researchers unprecedented insight into the complexity of the brain. Sim Shuzhen traces its development and asks where the technology could take us.

IOLOGICAL SYSTEMS ARE inherently complex, but the human brain perhaps outdoes them all. The brain is made of billions of neurons of every flavor, wired into intricate networks, firing on a millisecond timescale and influenced by a milieu of neurotransmitters and biochemical signals—small wonder then that we have little idea how this finely-controlled hive of activity translates into thought, emotion and behavior, or what exactly is different about the brains of patients with psychiatric disorders such as schizophrenia and depression.

The rapidly developing field of optogenetics, however, is providing scientists with tools that may finally be sophisticated enough to characterize this complexity. Optogenetic techniques let researchers control specific cell types using light and genetically-encoded, light-responsive proteins. With light, the manipulation is fast, spatially focused, and minimally invasive, a vast improvement from older techniques that used electrical stimulation or chemicals to perturb cells.

"The power of optogenetics is that it allows us to unravel the cellular complexity of the brain. There are hundreds, or even thousands, of different types of neurons and this makes it difficult to tease apart the function of each individual type of neuron," explained Professor George Augustine, an optogenetics researcher at the Synaptic Mechanisms and Circuits Laboratory of Nanyang Technological University, Singapore.

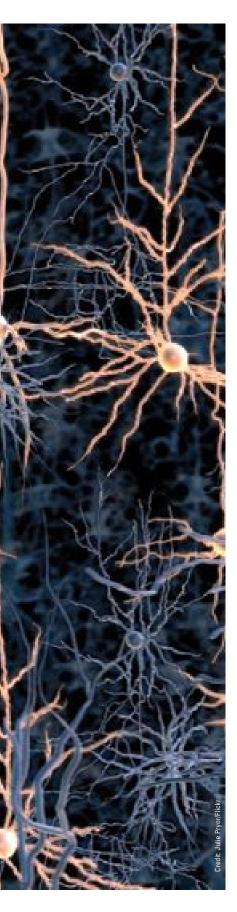
"Optogenetics nicely side-steps this problem by taking advantage of molecular genetic tricks to target expression of optogenetic probes to specific types of neurons. In this way, we can study the function of one genetically-defined type of neuron at a time," he told Asian Scientist Magazine.

From bacteria to brains

Discoveries in a field far removed from neuroscience would provide the basis for light-activated control. In 1971, researchers studying light-responsive bacteria identified bacteriorhodopsin, a light-activated ion pump that directly regulated ion flow across cell membranes.

Getting light-activated proteins to function in mammalian cells, however, was for a long time not attempted because it was considered almost impossible. One major question mark was whether or not mammalian cells contained all-trans retinal, a chemical co-factor required for opsins to function. Fortuitously, it turned out that all-trans retinal is naturally present in vertebrate tissue, and in a 2005 report, scientists led by Professor Karl





Deisseroth at Stanford University introduced the light-activated protein channelrhodopsin into mammalian neurons, showing that it alone made them fire in response to light. Other reports of optogenetic control in intact mammalian brain tissue and in live animal models soon followed over the next few years.

The optogenetic toolbox continues to grow as researchers characterize existing opsins in more detail and isolate new ones from bacteria and algae. Used in combination, opsins activated by different colors of light can be a valuable research tool. Putting one set of neurons under the control of blue light and another under the control of yellow light, for example, allows scientists to understand how each set affects behavior in a living animal.

Equally powerful is the ability to switch off neurons and observe the effect of this on behavior. This can be done with halorhodopsin, which hyperpolarizes cells in response to light, effectively silencing them. Researchers have also engineered mutations into opsin molecules to suit certain applications; making them work faster to keep pace with the brain's processes, or more slowly so that neurons are better able to respond to other stimuli.

Professor Hiromu Yawo, an optogenetics researcher at the Division of Neuroscience at Tohoku University, Japan, told Asian Scientist Magazine that his lab has engineered a rat that senses blue light as a touch to the skin, by introducing channelrhodopsin into neurons that activate mechano (touch) receptors. The group is now investigating how different spatiotemporal 'touch' patterns are represented in the brain, a task much more easily accomplished with light than with mechanical stimuli.

Applications in neurology

Optogenetics has now been used to investigate the neurological underpinnings of disorders such as depression, aggression, Parkinson's disease, schizophrenia and narcolepsy and often presents scientists with a more nuanced picture than

previously imagined. For example, researchers at Stanford University and the Mount Sinai School of Medicine found that activating the same set of neurons could make mice more or less depressed depending on the type of stress the animals had been exposed to prior to the experiment. This finding highlights the complicated nature of depression and may explain why antidepressants work for some patients but not for others.

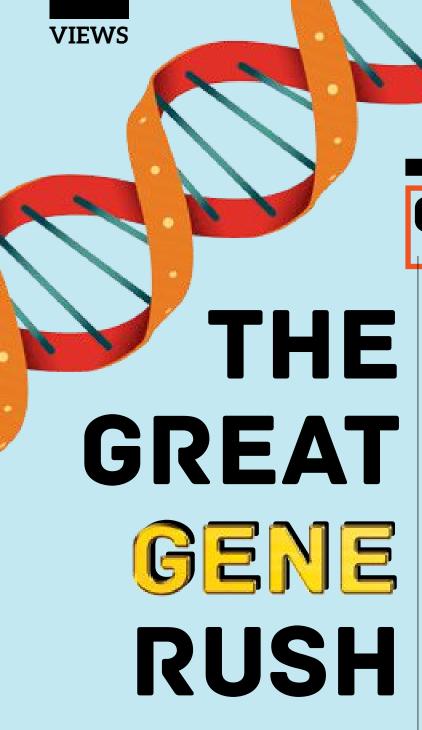
A major challenge for the field is that brain tissue scatters visible light, such that it does not penetrate very far below the surface. "This means that invasive devices such as optical fibers must be inserted into the brain if we wish to study the function of neurons that are one millimeter or more beneath the brain surface." said Augustine.

Light that borders on infrared wavelengths, on the other hand, penetrates tissues more easily and is more sharply focused. "If we could have optogenetic molecules (both actuators and sensors) that absorb near-infrared, we could manipulate neural activity from outside of the brain and record their activities also from outside," said Yawo.

Optogenetics is also rapidly finding applications outside of neuroscience. Many other cell types such as cardiac. muscle and pancreatic cells can be put under optogenetic control, offering researchers less invasive means of manipulation. At an even more micro level, researchers have used light to activate gene transcription and intracellular signaling cascades.

From its humble beginnings in bacteria and algae, optogenetics could someday drive a revolution in healthcare, by shining a light on the complex mysteries of the brain.

"RESEARCHERS HAVE **ENGINEERED RATS THAT SENSE BLUE LIGHT AS A** TOUCH TO THE SKIN."



Prospecting for patents

Forget gold, companies are now trying to make money from a rich new source—the human genome. But is this good or bad for research innovation?

Zaria Gorvett discusses.

N JULY THE 22nd, 1873, a tall, serious man sat down at his desk. He picked up his fountain pen, plunged it into the ink bowl, and wrote the following words: "Be it known that I, Louis PASTEUR, of Paris, France, have invented Improvements in the Manufacture and Preservation of Beer and in the Treatment of Yeast".

And thus begins the description of US patent 141072. Flanked by 141071, an improvement in furniture legs, and 141073, an improvement in wheel ploughs, this was no ordinary application. Monsieur Pasteur had invented an ingenious new way to purify brewer's yeast. However, not content with rights for the process, Pasteur was seeking to copyright the organism itself.

Natural phenomena such as gravity, minerals and wild organisms are strictly off limits for patents. But Pasteur had 'isolated' his yeast, detaching it from nature and turning it into a man-made product. As far as this French scientist was concerned, his innovation was no different from inventing a toaster or light bulb.

As it turns out, Pasteur's philosophy was a hit and scientists, entrepreneurs and patent lawyers have been enthusiastic patrons of biological patents ever since. Across the globe, companies have patented organisms and a cornucopia of molecules, including hormones, enzymes, vitamins, sugars, antibodies, proteins and controversially—genetic material.

Human genetic material is no exception. In fact, babies born in 2015 enter a world in which the rights to a fifth of their genes are owned privately, by universities and commercial enterprises. How did we get to this point?

First: what is a patent?

Patents are documents that protect new inventions in four general categories: a method, a machine, an article of manufacture, and a composition of matter.

The concept of patenting an idea is largely uncontroversial. By providing a competitive edge and helping companies to recoup their costs, patents encourage private investment. Patents on bacterial, viral or non-human animal genes are met with similar indifference.

Human gene patents, on the other hand, are seen differently. Detractors say they lead to an impenetrable legal tangle and high prices for diagnostics, and more crucially stifle important research. Proponents for patents keep to the traditional line, arguing that the commercial security they provide quickens medical innovation, ultimately saving lives.

Dollars from DNA

It began with a group of scientists with an ambitious idea: what if you could chart the genome of the human species, and create a map of all three billion letters of the genetic code? The Human Genome Project, as it was known, soon led to a private sector boom, with investors willing to bet the findings would lead to a deluge of new diagnostics and treatments. Gene patent applications rose from 4.000 to 500.000 in six years.

A year after the publication of the human genome data, Shanghai Joint Gene Technology Co. Ltd applied for more than 3,700 patents on genes involved in obesity, cancer, hypertension and dementia. In a healthcare market worth US\$357 billion in 2011, the rights to these genes mean big business.

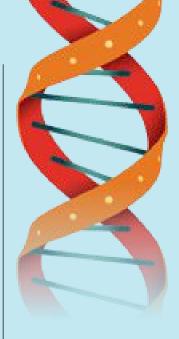
Copyright on cancer

The rules on what you can and cannot patent vary across the globe, but two landmark cases in the US and Australia have recently sharpened up the debate.

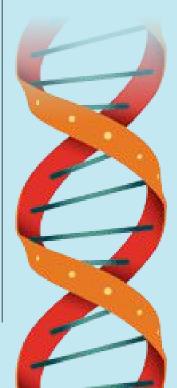
Both were filed against Myriad Genetics, a firm which provides genetic testing services. Among others, Myriad looks for BRCA1 and BRCA2 gene variants that are strongly linked to breast and ovarian cancer. It is an extraordinarily useful test: a mutation in the BRCA genes bumps one's lifetime risk up to 45-90 percent.

But at US\$3,000 the test wasn't cheap, and there was only one on the market. This is because, like Pasteur, Myriad Genetics didn't just patent their technology—they opted to patent the genes themselves. Naturally occurring genes, which had existed long before Myriad Genetics, patent law or the discovery of the structure of DNA, had become property. Was this just land-grabbing, or genuine value-adding?

The ensuing legal battle sought an answer. To argue their case, Myriad Genetics looked to Pasteur again. The genes were isolated from their natural environment, therefore they were an invention, they contended. They were unsuccessful. A judge of the United



THE RIGHTS TO A FIFTH OF OUR **GENES ARE PRIVATELY** OWNED.



States Supreme Court ruled that naturally-occurring DNA sequences are not patentable. However, a similar case tried in the Australian Federal Court reached the opposite conclusion.

Cancer Voices Australia, the patient advocacy group which filed the case, told Asian Scientist Magazine, "Cancer Voices is very disappointed in the recent Federal Court Decision. We understand that an appeal to the High Court is underway. [The ruling] will have a negative impact on research (delays, extra costs, less information), especially in the promising field of targeted therapies—something every cancer patient hopes to have good access to."

Limit patents, don't abolish them

Understandably, patients perceive gene patenting to be a major hindrance to treatment access. But should we discourage the patenting of genetic material? Intellectual property has a long history of encouraging innovation through investment. In the coming era of personalized medicine, are gene patents simply a pragmatic necessity?

"Overlapping patents on important gene sequences—also known as a patent thicket—tend to stifle downstream research and innovation. So in this case, more patents on a particular gene or technology are not always a good thing for long-term research and innovation, especially from the societal point of view," Kenneth Huang, professor of innovation and entrepreneurship at the Singapore Management University, told Asian Scientist Magazine.

"The key thing is to make the patentability bar—such as its novelty, inventive step and industrial applicability—high enough, and the scope of each patent narrow or specific enough, so as not to potentially deter downstream research and innovation."

The jury is still out on the patenting of genetic material, but perhaps the answer lies somewhere in-between. Until then, we will have to live with the uneasy knowledge that someone may already—or someday—own our genetic material.



New medical technologies could benefit patients, but adoption should always be tempered by cost concerns, said Dr. Ruben Flores at Medical Fair Asia 2014. **Rebecca Tan** reports.

ITH AN AGING population and rising incomes, Asia looks set to take a larger share of the global healthcare market. Consulting firm Frost & Sullivan predicts that the Asia Pacific region will account for a full third of the global healthcare market by 2015, worth a whopping US\$521 billion.

Catering to the increasingly sophisticated demands of Asian consumers, Medical Fair Asia 2014 brought some 200 exhibitors together to showcase the latest in diagnostics, medical equipment and medical technology and others. Into a successful tenth edition, the exhibition and concurrent Medical Manufacturing Asia 2014 conference was held at Suntec Singapore Convention and Exhibition Center from September 9-11, 2014.

Healthcare: a top priority for ASEAN integration

Kicking off the inaugural meeting with the opening speech was Dr. Ruben C. Flores, medical center chief of the Dr. Jose Fabella Memorial Hospital and president of both the Philippine Hospital Association and the Asian Hospital Federation. He stressed that the regional nature of emerging healthcare concerns demand an international response, a situation that the Association of Southeast Asian Nations (ASEAN) has taken steps to address.

"Life threatening illnesses like H1N1, SARS, MERS-CoV and Ebola virus must be contained and managed on a cross border basis. Because of the importance of collaboration in emergency healthcare situations, the issue of improving regional healthcare systems is one of the top priorities identified under ASEAN integration, set to take place in 2015," he added.

Speaking as a healthcare administrator with a regional perspective, he noted that technology is increasingly indispensable across Asia.

"The rapid rise in costs, increasing regulation, more intelligent and demanding consumers, the sheer number of providers and processes and fragmented health systems require the embrace of information technology in providing care," he said.

Planning for technology

However, it is one thing to recognize the need for technology and something else to start adopting technology on the ground. Particularly for an economically diverse region like ASEAN, the costs of new healthcare technology can be a major hurdle.

"The challenge for ASEAN is how to make healthcare available and accessible to member countries challenged by resource constraints." Flores said.

"Before we even think of investing in new technology, we need to build up a critical mass to ensure that the investment can be recouped; in effect, making the technology pay for itself. For this, we need to conduct a very careful study of the intended market."

"When it comes to managing the costs of healthcare on the other hand, we need to be aware that introducing a new technology can sometimes trigger off an arms race, where providers resort to driving unnecessary utilization and overpromising results in order to capture the market share."

Dr. Flores also highlighted that other hidden costs need to be taken into consideration when deciding to make a new investment in technology. These include operating cost, human resource, training, space allocation and other infrastructure improvements.

Looking to leaders

Even as healthcare decision makers seek to balance new healthcare technologies with rising costs, Dr. Flores reminded the audience of medical professionals of their fundamental roles as caregivers.

"Most importantly, we should remember that patients go to us not only for treatment but for healing. Thus, technology acquisitions should be balanced against making the hospital appear like an impersonal factory where automation replaces the warmth of the human touch. We must remember that no matter how advanced a technology might be, it can never ever replace caring hearts," he emphasized. \bullet

"WE MUST EMBRACE INFORMATION TECHNOLOGY IN PROVIDING CARE."

T

MEDICAL FAIR ASIA 2014 featured a wide range of innovative medical and health care devices, solutions and services



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What it takes to succeed in Asia's

biotech space



Ms. Kiran Mazumdar-Shaw, chairman and managing director of Biocon Limited, talks to **Yamini Chinnuswamy** about the challenges faced by biotech companies in Asia.

t's safe to say that Ms. Kiran Mazumdar-Shaw knows a thing or two about growing a successful Asian biotech company. Under her guidance, Indian biopharmaceutical company Biocon Limited grew from a two-employee operation in the 1970s into a billion dollar enterprise that seeks to deliver healthcare solutions across the biopharmaceutical innovation chain.

As for Mazumdar-Shaw, even though she started out in the brewery industry, her switch into the biotech space been successful enough to see her named as one of *Forbes* magazine's 100 most powerful woman in the world, and as one of the top 50 women in business by *Financial Times*.

The little biotech that could

"I've had many highlights in my journey with Biocon, starting with my success with enzymes manufacturing and my ability to transform that into a broad biopharmaceuticals business," Mazumdar-Shaw shared with *Asian Scientist Magazine*.

Biocon's first product was a plant enzyme known as papain, which is extracted from papayas and used in the fermentation of beer. Over the next few years, Biocon's industrial enzyme portfolio grew to include enzymes for textiles, biofuels and food products.

The Indian company would eventually divest its enzymes business, but in the interim, it grew a strong pipeline of biopharmaceuticals. Mazumdar-Shaw foresaw key opportunities in the patent expirations of drugs such as lovastatin, a cholesterol-lowering drug from Merck & Co., to develop generic versions that would be more affordable.

"We need biosimilars; we need generics. Without that kind of innovation, we will not be able to bring down the cost of drugs," she stressed. "It's a necessary kind of innovation, the kind that drives down costs."

That said, it was also clear to Mazumdar-Shaw that the way to tackle the many challenges of surviving in the biotech world would also require a commitment to innovation. Biocon has taken the approach of balancing "inventive innovation" targeting new drugs, remedies, therapies and other products, with the kind of innovation that gives the world biosimilars.

PEOPLE

"Most companies that go into biosimilars tend to focus on biosimilars. But our pipeline takes a bet on both biosimilars and innovative drugs. We believe the former will deliver predictable growth, while the novel products will develop non-linear growth," she added.

Unlocking Asia's growth potential

"The immense growth of our biopharmaceuticals business in turn allowed us to go public in 2004, which was a personal highlight and revelation," added Mazumdar-Shaw. "We were able to reach a one million dollar market cap on day one of our listing. It made me realize that in its first 25 years, our company had unlocked great value in India, Asia and the world."

She recognizes, however, that many other companies have not been so fortunate. According to Mazumdar-Shaw, the major issue faced by would-be Asian biotech companies today is the lack of access to capital markets where stocks, bonds, derivatives and other investments are traded. "Companies are unable access capital markets until they first attain a certain scale and size. This makes it difficult for biotech companies to invest in innovation."

"In the US, even start-up companies can access capital markets," Mazumdar-Shaw noted. "As soon as a company has a proof of concept, they're allowed to go to the capital market, and raise their next level of financing. This allows them to quickly scale up their technology, and make it to the market."

Innovation is gestational

Enabling access to capital markets will not be enough, however. Innovation is gestational, Mazumdar-Shaw opined, and the expectation of profit generation right after entering the capital market makes it more difficult for companies to develop and deliver on long-term strategies.

"These companies need time—say, three to four years—to advance. Of course, if a company fails, investors should exit from the stocks. Otherwise, it should suffice to ensure that a particular firm is making steady progress."

"It's possible that the Asian mind set is to reduce risk as much as possible," mused Mazumdar-Shaw, when asked why investors in Asia appeared to be conservative when it came to investing in regional biotech companies.

While such a philosophy to investment is practical, it is also why there aren't as many biotech companies in Asia able to hit the market as compared to the US, Mazumdar-Shaw explained. Which isn't to say there any companies, she was quick to point out; there are numerous small, innovative start-ups out there.

"One is a very interesting company called Strand Life Sciences, formerly Strand Genomics," she said. "They have a very big genomics story around their business. There's also another company called Sea6 Energy, which is trying to get into biofuels in a big way."

Many of these companies are eventually acquired by Western firms, she added, but Asian biotechs could be losing out by cashing out too early. "Western companies see the value in what these Asian start-ups are doing. Unfortunately, these Asian firms end up selling out at very low value."

Building credibility for Asia

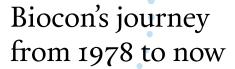
Despite the interest from investors, the impression of the world at large is that Asia does not have such a strong track record of innovation, according to Mazumdar-Shaw.

She is especially conscious of this perception as Biocon works to develop the world's first insulin tablet, allowing patients to do away with injections. "We are very confident that this can be done. It will be a fantastic product."

Mazumdar-Shaw was keen to emphasize that Asia has huge innovation potential. "Our Asian success stories—like Biocon, like Celltrion, like WuXi—should stand up and speak for themselves."

She added that Asia is ultimately the bigger market, and thus just as important as the US or European markets. "The world's growth markets are here. Everybody is eyeing the Asian market; it is ours for the taking."

The world's growth markets are here. Everybody is eyeing the Asian market; it is ours for the taking.



Biocon India is incorporated as a joint venture between Indian entrepreneur Kiran Mazumdar-Shaw and Biocon Biochemicals Ltd. of Ireland.

1979

Biocon is the first Indian company to manufacture and export enzymes to the US and Europe.

Unilever Plc. acquires Biocon Biochemicals Ltd. in Ireland. Biocon is the first Indian biotech company to receive US funding for proprietary technologies.

Biocon becomes an independent entity.

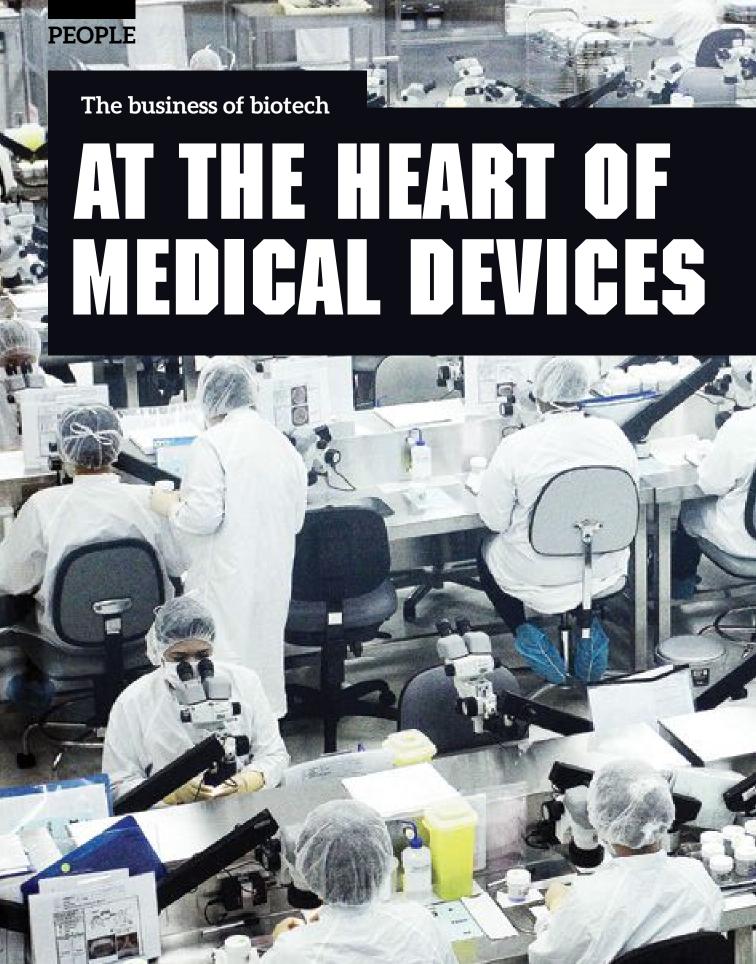
Biocon is the first company in the world to develop human insulin on a Pichia pastoris (yeast) expression system.

Biocon is listed on Indian stock exchanges as the first publiclyowned biotech company in Asia, achieving a one million dollar market cap on its first day of listing.

Biocon launches Basalog, a biosimilar of human insulin analog glargine, for type 1 and type 2 diabetes.

2014

Biocon introduces CANMAb. the world's first and lowest-priced biosimilar of Herceptin, to treat breast cancer in India.





Edwards Lifesciences is a leading medical device manufacturer, specializing in products for the treatment of structural heart disease and the critically ill. Asian Scientist Magazine catches up with Mr. Goh Khoon Seng, Asia Pacific director of professional education, heart valve therapy, to learn more about what makes the biotech industry tick. By Rebecca Tan.

What is your background and how did you enter the biotech industry?

GKS: I am a mechanical engineer by training. Upon graduating from the National University of Singapore I pursued my interest in medical technology and research. As an initiation into this field, I secured an attachment at the National University Hospital (NUH), which has a biomechanical lab that conducted tests on cadaveric limbs.

Sometime after that, I read in the papers that a start-up company in heart valve design and manufacturing was to be located in the Singapore Science Park. I visited them often, and spoke with them about their work. Upon seeing my passion in medical technology, I was offered employment there, and as the saying goes, the rest is history.

Was it a big jump going from mechanical engineering into medical devices?

GKS: Not at all. In fact, a lot of what we learn in engineering can be applied in the medical device industry. Heart valve function is basically about fluid dynamics. Our native heart valves, which are one-way valves, have no mechanism to activate their opening or closing. It's all mechanically activated by our blood flow and blood pressure.

There are two features important to the longevity of artificial tissue heart valves: the biomechanical aspect, which looks at strength and durability, and the biochemical aspect, which examines whether the material provokes an immune response or is inert.

What are the different types of heart valves available?

GKS: Edwards Lifesciences started as a heart valve company more than 50 years ago with the world's first replacement heart valve. This first valve, which was manufactured in 1958, was the Starr-Edwards valve. The valve has a ball and cage design that was the result of a partnership between engineer Miles "Lowell" Edwards and cardiac surgeon Albert Starr.

The next iteration was the Carpentier-Edwards porcine valve from a pig's heart, named after Alain Carpentier, a world renowned French cardiac surgeon and recipient of the 2007 Lasker Prize, along with Dr. Starr. The challenge in using valves from pig hearts was that the construction of the leaflets was not in our control and we had to make do with what nature sent out way.



PEOPLE





Currently, the most widely used valve is the Carpentier-Edwards PERIMOUNT bioprosthesis, which is a bioengineered valve using pericardial tissue from cows. Bioengineering provides us with the ability to develop the design of the valve, controlling factors such as stress, flexibility and leaflet quality. The leaflets are matched for thickness and elasticity and mounted on a flexible frame. Most recently, the technology has been utilized in the development of transcatheter aortic valves, which allow replacement without highly invasive open heart surgery.

What is the market for heart valves like?

GKS: In Asia where there are both developed and developing countries, there are two cohorts that need heart valve replacements.

In the developing countries, rheumatic fever is common, whereby \(\beta \)-hemolytic streptococci bacteria attack the heart valves and other tissues. Even long after the bacteria have been cleared with antibiotics, the body's repair mechanisms tend to thicken and calcify the tissue of the heart valve leaflets. As this process is gradual, patients may be stricken with rheumatic fever in their teens but only require surgery in their 30s or 40s. In a majority of these cases, it is the mitral valves that are affected.

The other segment of the heart valve market is in the developed countries where there are longer life expectancies. With this, patients present with degenerative heart disease and mainly the aortic valve is affected. Finally, there is congenital heart diseases that affect patients all around the world. These require valve surgery and constitutes 5–15 percent of open heart surgeries, depending on the country.

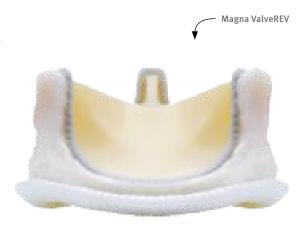
What are some of the factors that influence the adoption of new medical devices?

GKS: There are several factors that influence the adoption of new medical devices. Here are some for consideration: Firstly, the profile of the clinical specialty group. Secondly, the cost versus value of the new device, and lastly, revolutionary and evolutionary products.

In my experience, physicians in different clinical specialty groups vary in their technology adoption curve. Cardiac surgeons look for long-term outcomes, on the scale of 10-20 years, and often tend to take a conservative approach. Interventional cardiologists tend to be more receptive to new technology—such as drug eluting or bioabsorbable stents—and have a much shorter technology adoption curve.

That aside, I would say that most doctors are willing to accept new technology, but it is often the cost that limits the rate of adoption in some countries, particularly in developing countries. Cost effectiveness of a therapy is a factor that is scrutinized by payers such as the hospital administrators, health ministries and insurance companies. It is increasingly becoming part of the clinical trial process with new devices that the economics associated with the device must also be studied.

Revolutionary developments also influence the adoption of new technologies. For example, in the heart valve field, the transcatheter heart valve allows us to insert valves through the femoral artery. It takes time for us to develop the procedure and train doctors on a revolutionary product. Transcatheter heart valve therapy has created a lot of excitement among heart teams around the world, as it allows them to serve high risk patients who would face risks if treated with open heart surgery.





Why is training such an important part of marketing devices like heart valves?

GKS: Unlike pharmaceutical knowledge which is simply dispensed, there are skills associated with using medical devices. These skills can be complex or simple and this affects how readily the device and therapy is adopted.

Open heart surgery is not a single operator procedure but involves a whole team. There are a lot of people who we need to train, in addition to the doctors.

In Edwards Lifesciences the product is very much associated with meeting the needs of patients. It is important to us to provide the right training and information so that the doctors can make the right decision with the patient.

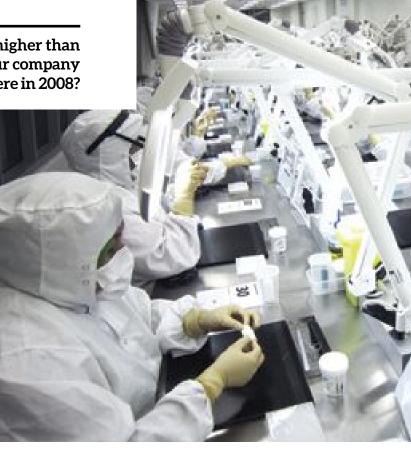


Human resource costs in Singapore are higher than elsewhere in the region. What made your company decide to set up a manufacturing plant here in 2008?

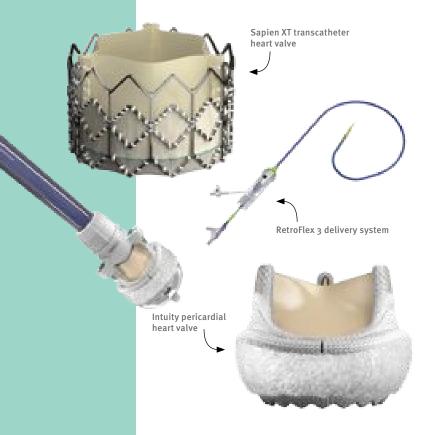
GKS: For high end medical devices like bioprosthetic heart valves, a skilled and dedicated workforce is necessary. The production volume is relatively small, in comparison to fast moving consumer goods (FMCG). In situations like this, the discipline of the workforce is of vital importance. We are not making a transistor radio or other consumer products—when dealing with medical implants such as heart valves, the devices must be of the highest quality and safe for patients.

There are many steps that are quite small and precise, suturing for example. In view of this, a culture of ownership and integrity is imperative. This is the kind of disciplined workforce that you will find in Singapore.

The other aspect that makes Singapore attractive for a medical device manufacturer like Edwards is that it is well known for good adherence to quality systems like ISO 9000 and specifically for medical devices, ISO 13485. Since 2005, we've been assessed by a number of regulatory bodies throughout the world and had very successful evaluations. This reputation makes Singapore a very important location for the manufacturing of medical devices.



PEOPLE



How can the regulation and registration of new medical devices be improved?

GKS: In Singapore, registration is relatively straightforward. However, it takes an average of one to two years. The regulators may need to review a lot of materials, treating each application as a totally new submission even though the product already has the CE mark or US Food and Drug Administration (FDA) approval.

In contrast, Thailand is very fast, giving approvals within two months. In places like Malaysia and Hong Kong, additional approval is not required for medical devices. In a majority of countries, it takes an average of nine months to one year to register a medical device.

In my opinion, patients would benefit from greater harmonization of the regulatory processes. Although each country has its own regulations, I believe there are more similarities than differences—if we can focus on better aligning these processes, then the costs and timeline could be reduced and medical devices can move into the country faster and start serving the patients.

Photo Credit: Edwards Lifesciences

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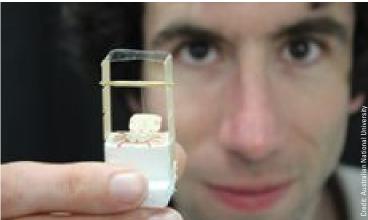
PANASONIC'S INDOOR FARM TO SUPPLY 5% OF SINGAPORE'S VEG

Panasonic has begun the commercial supply of locally-grown vegetables from land-scarce Singapore's first licensed indoor vegetable farm.

The 248m² indoor agriculture facility currently produces ten types of vegetables: green and red leafy lettuce, mizuna (potherb mustard), mini red and white radish, rocket lettuce, basil, ooba (mint herb), mitsuba (wild parsley) and baby spinach. The vegetables are cultivated in a controlled soil-based environment with LED lighting. At present, total production capacity is at

3.6 tons annually, or 0.015 percent of Singapore's vegetable consumption, with plans to increase to five percent by 2017.

"With over 90 percent of the food consumed in Singapore being imported, Panasonic hopes the indoor vegetable farm can contribute to the nation's food self-sufficiency levels and at the same time provide a better life and a better world through improved food quality," said Mr. Hideki Baba, managing director of Panasonic Factory Solutions Asia Pacific.



NEW MATERIAL PUTS A TWIST ON LIGHT

Scientists have uncovered the secret to twisting light at will, publishing their findings in *Nature Communications*.

"Our material can put a twist into light—that is, rotate its polarization—orders of magnitude more strongly than natural materials," said lead author Mr. Liu Mingkai, a graduate student at the Australian National University (ANU).

To obtain optical rotation, Liu and his colleagues used pairs of C-shaped metal pieces called meta-atoms, one suspended above the other by a fine wire. When light is shone onto the pair of meta-atoms the top one rotates, making the system asymmetric.

"It's another completely new tool in the toolbox for processing light," said co-author Dr. David Powell from ANU. "Thin slices of these materials can replace bulky collections of lenses and mirrors. This miniaturization could lead to the creation of more compact opto-electronic devices, such as a light-based version of the electronic transistor."

THIS PACEMAKER POWERS ITSELF

Scientists have developed a self-powered artificial cardiac pacemaker that may someday remove the need for surgery to replace pacemaker batteries.

Led by Professors Lee Keon Jae and Joung Boyoung from Severance Hospital of Yonsei University, the research team designed a flexible piezoelectric nanogenerator that directly stimulates the heart using electrical energy converted from the small body movements in rats.

The nanogenerators were engineered using a bulk single-crystal niobate-lead titanate thin film. Up to 8.2 V and 0.22 mA of energy could be harvested from bending and pushing motions, enough to directly stimulate a rat's heart. The results of the study have been published in the *Advanced Materials*.

Self-powered flexible energy harvesters may someday not only prolong the life of cardiac pacemakers but also perform real-time heart monitoring.

A BAND-AID FOR WEARABLE ELECTRONICS

Wearable electronics of the future could be powered by self-healing capacitors, thanks to research published in *Advanced Materials* by Dr. Chen Xiaodong from Singapore's Nanyang Technological University.

Flexible and wearable electronics must be able to endure repeated damage due to constant movement by the user without a loss in performance.

To design the self-healing supercapacitor, the group added an electrically conductive self-healing layer on top of a layer of current-collecting film that acted as the electrode. Whenever it was cut and re-joined, the self-healing layer acted as a glue, re-establishing current flow. The device was shown to work after five rounds of cutting and re-joining, with only a 15 percent loss in performance.

"This work may open new opportunities for the design and fabrication of various next-generation autonomous electronic devices with the capability of self-sensing, self-reporting and self-healing," Chen told Asian Scientist Magazine.

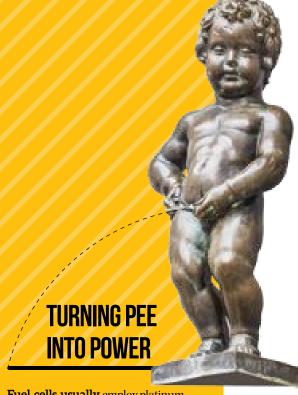
ABSORBING WATER FOR A CLEARER VIEW

Scientists have invented a permanent surface coating that attracts water instead of repelling it, producing clearer surfaces.

Researchers from the Institute of Materials Research and Engineering (IMRE) have invented a hydrophilic and transparent ceramic coating that is permanent, allowing surfaces on which the coating is applied to collect water and create a uniform and thin transparent layer.

Called *CleanClear*, the technology can be applied onto surfaces at processing temperatures below 100°C. Traditional titanium dioxide coatings can only be applied on surfaces during manufacturing processes that occur at temperatures above 600°C.

"CleanClear could be used to help create a sort of a clear 'vision shield' for today's car windshields during heavy rain," said Dr. Gregory Goh, the lead scientist from IMRE who developed the technology. "Or we could use it to replace current daytime, UV light-activated coatings with an all-day, all-night CleanClear coat on building facades to keep glass cleaner."

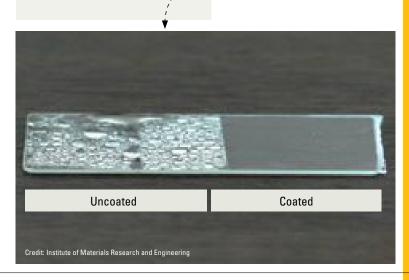


Fuel cells usually employ platinum (Pt) as an electrocatalyst to speed up their chemical processes. But the scarcity of Pt and its high cost have driven scientists to consider alternative electrocatalysts that are free of metals, such as carbon nanostructures. Carbon nanostructures, however, are highly specialized and difficult to synthesize.

Scientists from Korea University have now demonstrated that human urine is a potent source of carbon catalysts, which could help power supercapacitors and batteries.

Using a three-step process—dehydration, carbonization, and etching and washing—to purify samples of urine, they were able to synthesize porous urine carbon, which displayed catalytic strength comparable to the widely-used Pt catalyst.

"The findings should stimulate not only development of various novel carbon materials with superb functionality, but also extensive practical applications such as electrochemical electrode materials and adsorbents," the authors explained.



TECHNOLOGY WARRANGE CONTROL OF THE PROPERTY OF

ALUMINUM + CARBON FIBERS = STRONG AS STEEL

Stronger than aluminum, but cheaper and lighter than steel, researchers at the Hong Kong University of Science and Technology (HKUST) and aluminum manufacturer UC RUSCAL have used nanotechnology to integrate carbon fibers with aluminum.

The fiber reinforced aluminum (FRA) could be used to produce building envelope systems that are safer, cheaper, more energy-efficient and easier to mount.

"FRA is a mixture of carbon fiber and aluminum. If used together with

a phase-change material, it creates a smart building envelope system which will effectively reduce indoor temperature fluctuation and halve the labor costs and construction time compared to conventional systems built mainly from steel and cement," said Professor Chan Yui-Bun from HKUST.

FRA can be used for a wide range of applications primarily in construction as an alternative to steel and cement, and also in electronic products, automobiles, aircrafts and building materials.

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PER SECOND

Physicists at the University of Tokyo have devised a new way to film videos of processes that last only trillionths of a second.

Their method, dubbed sequentially timed all-optical mapping photography (STAMP), has been published in the journal *Nature Photonics*.

First, a laser passes through a "temporal mapping device" that makes use of a slight spread in the wavelength of the laser light. Slightly longer wavelengths of light take less time to pass through the temporal mapping device, causing the laser

light to be separated into successive short pulses. Each pulse hits the target at a slightly different time, creating successive individual images; the pulses are then mapped spatially to reconstruct the image.

Using STAMP, the researchers were able to capture footage of a single phonon at a resolution and speed sufficient to observe important details. It is anticipated that the camera will also be useful for studying fast dynamics in fields such as photochemistry, spintronics and plasma physics.



Credit: Keisuke Goda/University of Tokyo



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February Michigan Contract



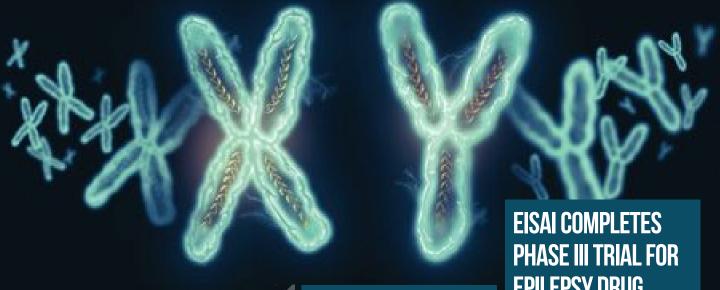
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PHARMA



BGI'S DOWN SYNDROME TEST GETS CFDA APPROVAL

In a reversal of a previous ruling banning clinical genetic testing, the Chinese Food and Drug Administration (CFDA) has approved BGI's non-invasive fetal trisomy test (NIFTY) for fetal chromosomal aneuploidy.

The test makes use of cell-free fetal DNA in the maternal blood of high-risk pregnant women after 12 weeks of pregnancy. It can detect fetal chromosomal aneuploidy diseases including Trisomy 21 (Down Syndrome), Trisomy 13 (Patau Syndrome) and Trisomy 18 (Edwards Syndrome).

In early 2014, CFDA and the National Health and Family Planning Commission announced their intention to regulate clinical genetic testing, banning all clinical genetic testing except for projects under the government. The approval of BGI's diagnostic kits comes as a relief to BGI and other diagnostics companies hoping to enter the Chinese market.

FIRST DRUG FOR DEMENTIA WITH LEWY BODIES APPROVED

Eisai Co. Ltd's anti-Alzheimer's agent Aricept® (donepezil hydrochloride) has received approval for a new indication for dementia with Lewy bodies (DLB) in Japan. This marks the first time a treatment has been approved for DLB anywhere in the world.

DLB was discovered in 1976 by Dr. Kenji Kosaka, Professor Emeritus of Yokohama City University. It is a degenerative form of dementia that is pathologically characterized by a decrease in neurons in the brain and brainstem and the appearance of vast numbers of inclusions known as Lewy bodies. However, DLB is difficult to diagnose because of the overlap in symptoms with diseases such as Alzheimer's and Parkinson's.

Eisai will carry out an observational study to gather data on long-term use, and perform an additional clinical trial to confirm efficacy of Aricept for this additional indication.

Eisai Co. Ltd. has concluded a Phase III

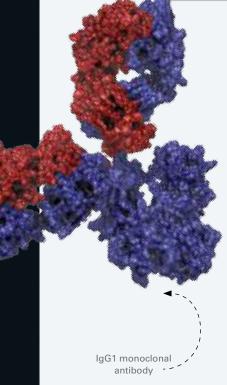
clinical trial of its in-house-discovered AMPA receptor antagonist Fycompa® in patients with primary generalized tonic-clonic (PGTC) seizures, one of the most severe forms of generalized seizures.

Epileptic seizures are primarily mediated by the neurotransmitter glutamate. Fycompa is a highly selective, noncompetitive AMPA receptor antagonist that reduces neuronal hyperexcitation associated with seizures by targeting glutamate activity at postsynaptic AMPA receptors.

The study was a double-blind, randomized, placebo-controlled, multicenter, parallel-group study to evaluate the efficacy and safety of adjunctive Fycompa therapy in 164 patients aged 12 years and older with uncontrolled PGTC seizures receiving one to a maximum of three anti-epileptic drugs.

Based on the results of this study, Eisai plans to submit applications to health authorities in the EU and the US for an indication expansion to include the adjunctive treatment of PGTC seizures. A clinical study on patients with partial-onset seizures is also currently underway in Asia.

A*STAR & ROCHE DEVELOP CANCER KILLING ANTIBODIES



A*STAR's Bioprocessing Technology Institute (BTI) has entered into an agreement with Swiss pharmaceutical company Roche to identify antibodies that can target and directly kill cancer cells.

Cancer cells may be distinguished from normal cells by their elevated levels of sugar on the cell surface. A set of monoclonal antibodies (mAbs) engineered by BTI are able to recognize these sugar targets and allow for more accurate identification of cancer cells as compared to traditional antibodies that only target proteins. The mAbs are also unique in that they cause pores to form on the surface of cancer cells, leading to cell death.

BTI's partnership with Roche will allow new diagnostic tests and cancer treatments to be developed based on these mAbs.

GILEAD HIV GENERICS FOR INDIA & CHINA

An agreement with the Medicines Patent Pool (MPP) allows generics manufacturers in India and China to produce Gilead's Hepatitis B and HIV drug, tenofovir alafenamide (TAF).

In addition to its agreement with the MPP, Gilead has direct partnerships with 11 generic manufacturers. Due to competition among these generic drug manufacturers, the lowest price of a Gilead HIV medicine has fallen 80 percent since 2006, to US\$4.00 per patient per month.

Currently 5.4 million people are receiving Gilead HIV medicines in low- and middle-income countries, more than half of all people on HIV therapy in these countries.

LUYE RAISES US\$764 MILLION WITH HONG KONG IPO

Chinese pharmaceutical Luye Pharma has raised US\$764 million through an IPO on the Stock Exchange of Hong Kong. Luve's share price closed at HK\$6.7 (~US\$0.86), up 13.2 percent from the offer price. The company manufactures and sells drugs for the treatment of cardiovascular disease and cancer.

Executive Chairman and CEO of Luve, Mr. Liu Dian Bo said, "As the largest Hong Kong pharmaceutical IPO for the past two years, the Company's strong share price performance today reflected investors' favorable view on the prospect for the Company and the capability of our senior management."



BioPharma ASIA CONVENTION 2015

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A Night Of Celebration

Asian Scientist Magazine's First Year In Print











in print, you can guarantee that a party was in store at Asian Scientist Magazine.

in print with a cocktail celebration at Suntec Singapore Convention & Exhibition Centre.

Singapore, the event was attended by media partners, friends and colleagues.

SPRING Singapore Chairman Mr. Philip Yeo, with Mrs. Doreen Phua, managing director of World Scientific Publishing Company (WSPC), also in attendance.

Philip Yeo, who congratulated the team at Asian Scientist for the launch of their print magazine, followed by Dr. Juliana Chan, editor-in-chief of Asian Scientist Magazine, who charted the magazine's trajectory since it began in 2011.

was Mr. Max Phua, executive director of WSPC, who commended Asian Scientist's efforts to nurture a science communications industry in Asia.

"I think there are two reasons that Asian Scientist is doing so well: First, they have found a specific niche and they are staying true to their vision, which is to cover Asian science, focusing on Asia and Asian researchers," said Mr. Phua. "Second, the magazine is curated by professional scientists and experienced science journalists, which means that they are writing for their peers, and trusted by their peers."

With a successful first year in print, the team at Asian Scientist is hoping for more bumper years to come. See you next year!









- 1. Dr. Toh Yi Kai, WSPC editor, and Dr. Tang Yew Chung, Asian Scientist editor
- 2. Mr. Goh Chien Yen and Dr. Rebecca Tan, Asian Scientist managing editor
- 3. Mrs. Doreen Phua, Dr. Juliana Chan, Dr. Lee Pei Ming and Mr. Max Phua
- 4. Mr. Goh Yong Sheng and Ms. Janice Goh from Suntec Singapore, with Ms. Yvonne Tan, senior manager at the Singapore Management University Office of Research
- 5. Mr. CH Kong, senior director of marketing and product development at Suntec Singapore, Dr. Juliana Chan, Mr. Philip Yeo and Mr. Max Phua
- 6. Dr. Howard Califano, director of the Singapore-MIT Alliance for Research and Technology (SMART) Innovation Center and Dr. Chester Drum, Asian Scientist advisor
- 7. Clara Wong, Asian Scientist marketing manager (middle), with Ms. Carol Lau (L) and Ms. Marina Yusof (R) from Frasers Hospitality
- 8. Dr. Virgina Cha, entrepreneur and angel investor, and Mr. Kimo Cummings

B LIFE: IT TAKES

Lab characters that you either love or loathe.

It is a truth universally acknowledged that every lab has the same people in it, no matter which lab you're in. While there may be slight variations, here are some of the key people in your lab and how to spot them. By Alice Ly.



THE BIG BOSS

The name that names your lab. The name that signed your contract. The name at the end of your papers. But the reason why I'm referring to the Big Boss as 'The Name' is because they're probably shuttling between their many labs or traveling to international conferences and you don't actually see them much other than their name.

How to spot them:

By the look of fear and hurried actions of people when they realize that the Big Boss is on campus today and wants to talk to them.



THE ACTUAL BOSS

While the Big Boss is globetrotting, this is the person who you really discuss work with and who you really answer to. Highly trusted by the Big Boss to keep the lab running smoothly while they're not there, the Actual Boss is usually a PI who doesn't do their own work anymore because they are too busy attending meetings on the Big Boss' behalf.

How to spot them:

Usually in their office writing grants for the Big Boss.

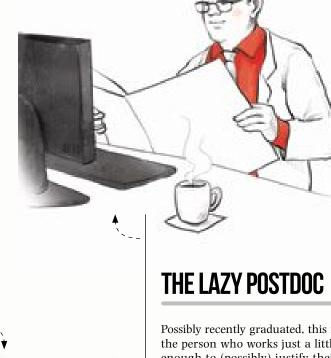
ALL KINDS

THE SUPER POSTDOC/ **PHD STUDENT**

These people have been around long enough to know where everything is in the lab, all the techniques, and who to ask on campus if you want access to a special machine. One rung below but with less stress, Super Postdocs may often turn into the Actual Boss. However, the Super PhD may decide to leave the lab as they see that the position of Super Postdoc is already filled.

How to spot them:

Demonstrating the use of a machine, how to do a dissection, or happily looking at and discussing your data.



Possibly recently graduated, this is the person who works just a little enough to (possibly) justify their position and salary, but more likely enrages everyone by arriving late, leaving early and taking vacations, making you all wonder what it is they actually do. If you were present at the time of their hiring, you possibly wonder to this day how they worked enough to get their PhD and what kind of black magic was cast during their job interview.

How to spot them:

Drinking coffee in the tea room or reading the newspaper at their computer.





THE AMBITIOUS PHD

The Ambitious PhD works long, works hard and works well. They'll look at disparate pieces of data and suddenly pull it all together to come to conclusions that make perfect sense. This often means that they are rewarded with jealousy-inducing high impact papers, but you always feel a bit of thrill when they ask you if you can contribute an experiment to their study because that means you'll also be an author! The Ambitious PhD isn't concerned with popularity though and is often rewarded with postdoc positions in prestigious universities.

How to spot them:

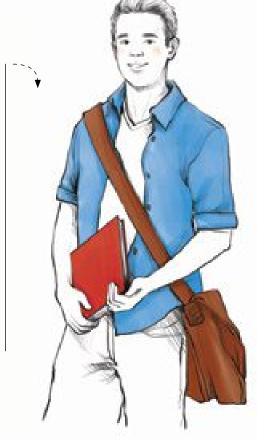
On the stage, receiving awards.

THE UNDERGRAD/ **INTERN STUDENT**

These young and shiny ambitious people thought that they would like to experience working in a lab. Then they discovered that TV lied to them and that PCRs can't tell you the name of whose hair was found on the towel at the crime scene.

How to spot them:

The look of confusion on their face as they read a protocol or look at the collection of different bottles to make assorted buffers.





THE SENIOR TECHNICIAN

This person has seen them come and seen them go. They are probably the master of a specialized technique like electron microscopy or a Machine Whisperer and therefore cannot and never will be fired. Usually friendly and happy to demonstrate their area of expertise, beware of ever getting on their bad side.

How to spot them: By their lab coat.



THE ENGINEER/ IT PERSON

If your group is lucky enough to have one these people, you better thank your lucky stars and start learning how to make their favourite food. This is the person you call to offer your first born child when a machine repeatedly flashes an error signal or when your computer won't load the data you spent 18 hours collecting yesterday.

How to spot them:

All the technical hardware and cakes on their desk, given to them by grateful researchers for recovering their data or fixing a machine.

THE BIG BOSS' PA

Although technically not part of the lab and probably never a scientist, if this person is there, they are likely to be the most powerful person in the lab. As the controller of the Big Boss' schedule and possibly keeper of finances, they can make or break when your project progress report is due and if there is enough lab money available for you to buy enough reagents to complete your experiment.

How to spot them:

By their organized look and their ability to pull up the appropriate calendar or spreadsheet to answer your question.



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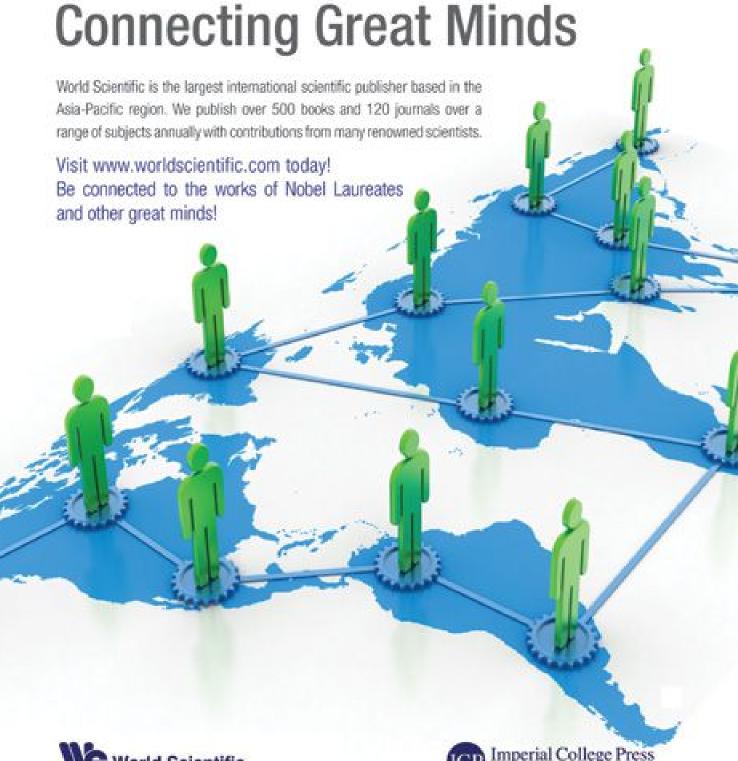
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Steps To Starting A Biotech Company

It is by no means easy to start any company, more so a biotechnology company where the barriers to entry are high and the risks are formidable. However, the goal of making a tangible difference to the lives of consumers has attracted many to the scene. Here are seven steps that most biotechnology start-ups take:

Make absolutely sure that your idea has a true market need

Good ideas are just that: good ideas. At this stage, it is absolutely crucial that you speak to scientists, venture capitalists and any potential customers to assess whether there is a genuine market need for your product.

Identify founders and key personnel

Look for people who share your vision for the company, and who see themselves as stakeholders rather than just employees.







Conceive a business plan and marketing strategy

Your technology might be revolutionary, but be realistic about how much it will cost to bring your product to market, what your business model is, and whether your product is truly unique.

Find a good attorney and incorporate your company

Incorporating your company protects you, the founder, from liabilities incurred by the company and makes it easier for you to raise capital through the sale of equity.

Bootstrap until you reach proof-of-concept

Don't quit your day job! Keep your expenses low and work towards a minimum viable product.

Find paying customers and/or raise seed capital

Bootstrapping has its limits, of course. It is crucial that you are continually on the lookout for new streams of revenue.

Advance the technology through successive product development milestones

Which brings us to our last point. It is important that you set tangible, achievable development milestones to boost investor confidence and make it easier for you to secure your next round of funding.





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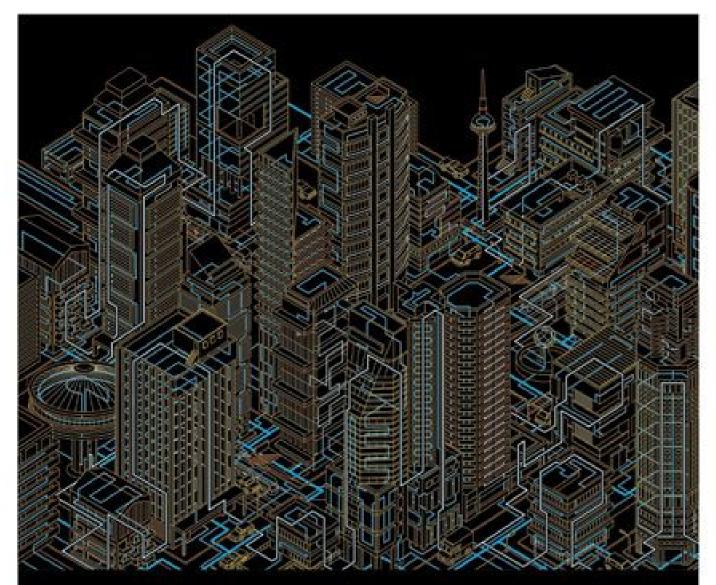
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